CLAIMS

What is claimed is:

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A method for identifying an anti-viral agent comprising:
 contacting a NS4B nucleotide binding motif (NBM) polypeptide with a candidate
 agent; and

determining an effect of said candidate agent on a nucleotide binding activity, a nucleotide hydrolyzing activity, or a nucleotide-dependent RNA binding activity of said polypeptide.

- 2. The method of claim 1, wherein said NS4B NBM polypeptide is a hepatitis C virus (HCV) NS4B NBM polypeptide
- 15 3. The method of claim 1, wherein said determining comprises determining an effect of said candidate agent on nucleotide binding of said polypeptide.
 - 4. The method of claim 1, wherein said determining comprises determining an effect of said candidate agent on an ability of said polypeptide to hydrolyze a nucleotide.
 - 5. The method of claim 1, wherein said determining comprises determining an effect on an RNA binding activity of said polypeptide.
 - 6. The method of claim 1, wherein said candidate agent is a nucleotide analog.
 - 7. The method of claim 6, wherein said nucleotide analog is a non-hydrolysable nucleotide.
- 8. The method of claim 1, further comprising determining an effect of said candidate agent on replication of HCV.
 - 9. The method of claim 4, wherein said HCV is a subgenomic or full length HCV replicon.

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10. The method of claim 1, further comprising testing HCV replication in a huh7 cell.

- 11. A method for modulating NS4B protein activity, said method comprising:
 contacting said NS4B protein with a modulatory agent in an amount sufficient to
 5 modulate a nucleotide binding activity, a nucleotide hydrolyzing activity, or an RNA binding activity of said NS4B protein.
- 12. A method of inhibiting HCV replication in a cell, comprising:
 contacting a cell infected with HCV with an NS4B polypeptide inhibitor, wherein
 10 said contacting inhibits a nucleotide binding activity, a nucleotide hydrolyzing activity, or an RNA binding activity of said NS4B polypeptide of said HCV and thereby inhibits HCV replication in said cell.
 - 13. The method of claim 12, wherein said HCV is an HCV subgenomic replicon.
 - 14. The method of claim 12, wherein said cell is a huh7 cell.

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- 15. A polynucleotide encoding a HCV NS4B protein with reduced nucleotide binding activity.
- 16. The polynucleotide of claim 15, wherein said polynucleotide encodes a polypeptide comprising the sequence $X_1X_2X_3X_4X_5X_6X_7$, where X_1 is an amino acid other than Gly, X_2 is an amino acid other than Ser or Gly, X_3 is an amino acid other than Ile or Val, X_4 is an amino acid other than Gly, X_5 is an amino acid other than Leu or Ile, X_6 is an amino acid other than Gly and X_7 is an amino acid other than Lys or Arg.
- 17. A virus particle containing the polynucleotide of claim 15.
- 18. A method of treating a subject for hepatitis C, comprising:

 administering to said subject an agent that inhibits nucleotide binding activity, a

 nucleotide hydrolyzing activity, or an RNA binding activity of an HCV NS4B polypeptide in
 an amount effective for the treatment of said subject.
 - 19. The method of claim 18, wherein said subject is a human subject.

20. The method of claim 18, wherein said agent is administered in combination with another anti-HCV agent.

21. The method of claim 20, wherein said agent is ribavirin or interferon.

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